Supporting Information for: *in silico* Exploration of Molecular Mechanism of Clinically Oriented Drugs for Possibly Inhibiting SARS-CoV-2's Main Protease

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Supplementary Movies

Supplementary Movie 1 (entecavir.mpg): showing the simulation trajectory of entecavir in the Mpro's pocket.

Supplementary Movie 2 (nelfinavir.mpg): showing the simulation trajectory of nelfinavir in the Mpro's pocket.

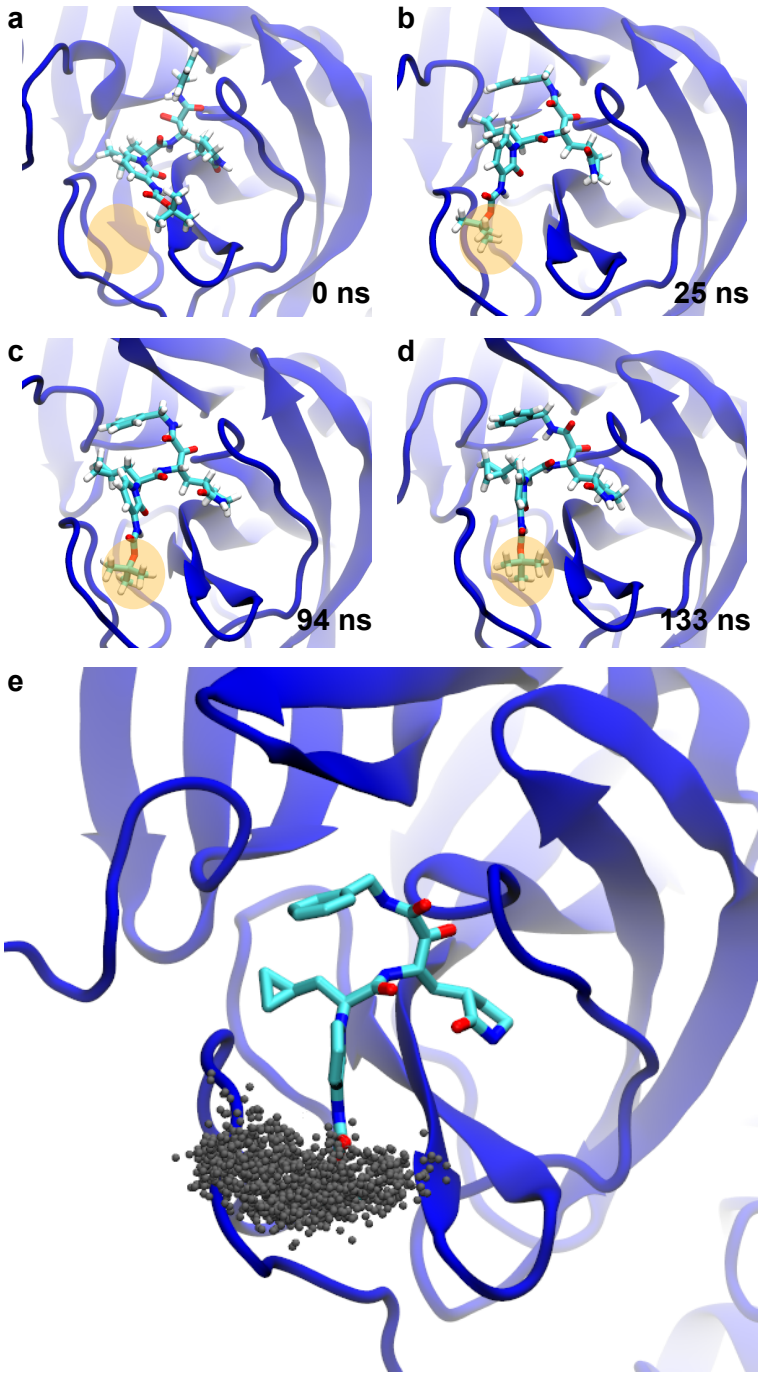

Figure S1: MD simulation of O6K inside the Mpro's pocket. a-d) Snapshots of the O6K molecule inside the Mpro's pocket when t=0, 25, 94 and 133 ns. The pose of O6K in the crystal structure is shown in (a), illustrating that the BOC group of O6K is not inside the "anchor" site due to a DMSO molecule that was removed in MD simulation. The simulation system size is about the same as that for entecavir and we applied same simulation protocols. The orange oval shows where the "anchor" site is. e) An enlarged view illustrating all possible positions (gray dots) of the hydrophobic -C-$(CH_3)_3$ group in O6K from the MD simulation.

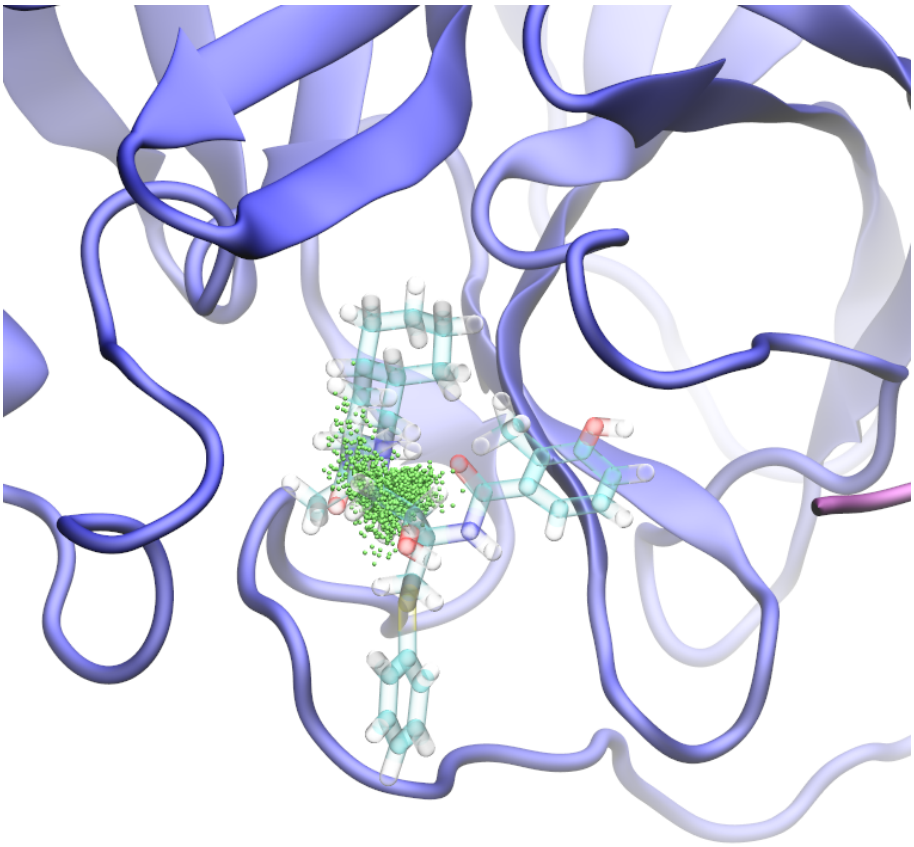

Figure S2: A snapshot of nelfinavir in the Mpro's pocket from the second MD simulation (Sim-2), which is consistent with what we found from Sim-1. Green dots show the distribution of nelfinavir's positions during the MD simulation.